PEDIATRIC TB

Modified PPT from group A seminar (F)
Objectives

• the epidemiology of pediatric TB.
• TB Mycobacteriology.
• pediatric TB presentations compared to adults TB.
• Know the differences between, and isolation guidelines for, patients with LTBI and active TB.
• guidelines for pediatric TB workup and management.
• TB treatment.
Epidemiology

Of the ∼1 million estimated cases of TB in children worldwide, 75% occur in the 22 high-burden countries. In low-burden countries, childhood TB constitutes ∼5% of the TB caseload, compared with 20%–40% in high-burden countries.

Regional data from the World Health Organization (WHO) in 2007 showed that smear-positive TB in children aged <14 years accounted for 0.6%–3.6% of reported cases. However, because ∼95% of cases in children <12 years of age are smear negative, these data underestimate the true burden of TB.
Epidemiology

Furthermore, in countries with a high prevalence of HIV infection, there has been a marked increase in the incidence and a decrease in the peak age prevalence of infectious TB; thus, most cases now occur in young adults, who are often parents of young children. This finding suggests that children in developing countries will emerge as a group at high risk; in fact, in 2007, the majority of children with smear positive TB who were <15 years of age were in Africa and Southeast Asia.
MYCOBACTERIOLOGY

*Mycobacteriology criteria:
G –ve bacilli aerobe, non sporing, capsulated and non motile.
*measures: width 0.3-0.6 nm & length 1-4 nm.
*the only organism that cause TB in human known as tubercle bacilli are: M. tuberculosis, M. bovis, M. africanae (Typical TB).
M. leprosy (Atypical TB).
MYCOBACTERIOLOGY

Staining

Z-N stain; known as AAFB (cord growth).

* Fluorescent dyes.
MYCOBACTERIOLOGY

- culture:* (L-J media (rate of growth 2-6 w)
- *Bactec media (10-14 d).

- Optimal growth required:
- Temp. 33-38 C, PH 6.5-6.8, and Atmosphere
- 5-10 % CO2.
characters of the organism:
1- lipid rich cell wall of mycobacterium
Eight Week Growth of *Mycobacterium tuberculosis* on Lowenstein-Jensen Agar.
pediatric TB presentations compared to adults TB
Childrens are ( Important )

1- Tend to develop primary active TB more often after initial infection (0-4yrs)
2- Are more likely to have extrapulmonary disease, especially TB meningitis (0-4yrs)
3- Are more likely to have disseminated TB infection
4- Are less contagious
   Paucibacillary disease (fewer organisms)
   Cannot cough/spread infection as well
5- Are more difficult to diagnose
   May not show typical symptoms
   May have TB disease in unexpected places
Symptoms

1-Hemoptysis (bloody sputum)
2-persistent fever,
3-night sweats with a nicely diagnostic CXR is largely a myth in Peds, especially <5yrs
Presentation

**Symptoms are usually nonspecific**

Poor appetite, weight loss, failure to thrive, intermittent fevers, +/-cough, listlessness, decreased activity, irritability (TB meningitis)

*Persistent cough > 2 weeks, failure to thrive, fatigue* were best indicators in a study done in 1000+, non HIV infected children in S Africa

Other studies have had similar findings

For extrapulmonary TB, think of additional signs and symptoms based on site of disease eg lymph node, kidney, bone, brain
Source of infection: adult contact who is suffering from pulmonary T.B

Outcomes

Inhalation and deposition of the tubercle bacillus in the lungs leads to one of four possible outcomes:
Type of TB Diseases (Important)

1/ Immediate clearance of the organism

2/ Chronic / latent infection

3/ Rapidly progressive disease / primary disease

4/ Active disease many years after the infection (reactivation disease) (occur in 5 - 10% of patients)
Latent TB

- Positive PPD and negative CXR
Active TB

- Positive PPD and Positive CXR
Formation of primary complex

1- Child inhales tubercle bacilli down to the alveoli and pass to the interstitial tissue

2- Accumulation of poly morphonuclear leukocyte then epithelioid cells, these surround the tubercle bacilli forming typical tubercle, some of epitheliod cell fuse to form giant cell when hypersensivity develops, the tuberculs become surround by the lymphocyte

- Central **caseous necrosis** is commonly present.
Primary infection (Caseating granuloma)
Primary infection TB

This primary focus in lung is called Ghon’s lesion, usually single but may be multiple, situated subpleurally, 1cm in diameter.

The bacilli travel via the per bronchial lymphatic towards the broncho-pulmonary and tracheobronchial lymph node. Ghon’s lesion, lymphangitis, hilar lymphadenitis, constitute the primary complex.
Clinical picture of primary complex

A- usually pass unnoticed
   b- Manifestations of hyper sensitivity to tuberculoprotein (4-6 weeks)

Manifestations include
1- fever, low grade may last for 3-4 weeks
2- phlyctenular conjunctivitis
3- erythema nodosum
4- pleural effusion
Extrapulmonary Manifestations of primary TB

- Erythema nodosum
- Phlyctenular conjunctivitis
Fate of primary pulmonary complex

It depends on the virulence of organism
And the state of immunity.

A-healing: by fibrosis and calcification, some time the organism remains dormant to be activated later on when immunity diminishes.

B-complication by spread of organism either locally, by bronchial tree or by the hematogenous route.
Acute Miliary TB:

C/P:
- Very severe general symptoms: wasting, anorexia, pallor & high temperature.
- Symptoms of lung involvement e.g. cough, wheeze.
- Hepatosplenomegaly.
- Choroidal tubercles by fundus examination.
- X-ray chest: miliary shadows (snowstorm appearance.)
Spreads of TB:

- Local spread gives rise to:
  - 1- Locally extending Ghon’s lesion.
  - 2- Enlarged mediastinal lymph glands.
  - 3-segmental lesions.

- Spread via the bronchial tree.
- Spread via blood stream.
Miliary TB
<table>
<thead>
<tr>
<th></th>
<th>Acute / classical miliary TB</th>
<th>Cryptic miliary / disseminated TB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Children</td>
<td>Elderly</td>
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<tr>
<td><strong>Onset</strong></td>
<td>Acute / subacute febrile illness</td>
<td>Insidious</td>
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<tr>
<td><strong>Features</strong></td>
<td>1/ Vague ill-health</td>
<td>1/ Pyrexia of unknown origin (PUO)</td>
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<tr>
<td></td>
<td>2/ Systemic involvement</td>
<td>2/ Weight loss</td>
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<tr>
<td></td>
<td>3/ Choroidal tubercles</td>
<td>3/ Malaise</td>
</tr>
<tr>
<td></td>
<td>4/ Variety of blood dyscrasias</td>
<td></td>
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<td></td>
<td>5/ Disturbed liver function tests</td>
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</table>
TB of Meningitis

This is the **principal cause of death** from TB in the 1\textsuperscript{st} year of life.

Discharge of TB bacilli into CSF from caseous foci as a tuberculoma in the brain, spinal cord or osseous lesion of the vertbrae but may be involved by the hematogenous spread.
C/P

• This is divided into 3 stages:
  • 1- prodromal stage
  • 2- stage of meningitis
  • 3- terminal stage
ISOLATION
Patients with initial sputum smear-positive for Acid Fast Bacilli (AFB)

Home Isolation*

For patients with at least one positive AFB smear from sputum, and high clinical suspicion, of TB and a presumed pansensitive organism, regardless of chest x-ray findings, home isolation may be considered, when all of the following criteria are met:

1. Household with previously exposed children younger than five years of age
2. Household with previously exposed immunocompromised individuals five years of age and older
3. Household with previously exposed immunocompetent individuals five years and older
ISOLATION

Latent TB:

No isolation because he Cannot spread TB bacteria to others
Isolation

- Active TB

- Isolation in negative-pressure room with Airborne TB precautions (fitted N95 mask)
diagnosis

1. **History** of contact with adult with TB

2. **physical examination:**

   Loss of weight, fever, night sweat, anorexia, easy fatiguability, sign of obstructive hyperinflation, collapse, consolidation, efusion or bronchopneumonia.
Investigation

1. Blood test:
   a/ White blood cell count
   Normal with relative lymphocytosis
   If it increases indicate Secondary Bacterial Infection
   b/ Haemoglobin :: Normochromic normocytic anaemia
   c/ ESR = raised

2. Liver & renal Function Test
   Should be done before initiation of treatment

4. C-Reactive Protein (CRP): Raised

5. HIV serology: Should be obtained for all patients with TB.

6. In TB meningitis: CSF analysis

7. ELISA for diagnosis of TB antigen
• 6. Sputum <8yrs don’t do sputum very well)
• 1/ Staining
  • a/ ZN stain
  • b/ Fluorochrome stain
• 2/ Culture Is the gold standard for the definitive diagnosis of TB
• 3/ Polymerase chain reaction (PCR)
  • capable of detecting a single organism in a specimen of sputum

• **Gastric aspirates**: they cough up the TB bacilli, then swallow them into the stomach
  • Perform every morning for 3 days-need admission
Purified Protein Derivative (PPD) test

A-Purified protein extracts from TB cultures are injected into skin

B-Immune T cells that have been sensitized to TB from prior infection migrate to the injection site

C-Release chemicals that produce local inflammation and induration (bumpy reaction)

D-After initial infection, it takes 2-10 wks (median 3-4 wks) to develop hypersensitivity to the PPD test.

E-At best, PPD is ~90% sensitive, ~90% specific
## Definitions of positive PPD (Red Book 2009, p 681)

<table>
<thead>
<tr>
<th>Categories</th>
<th>Measurement cut-off</th>
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<tbody>
<tr>
<td>1. Child in close contact with known or suspected contagious TB case</td>
<td>≥5mm</td>
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<tr>
<td>2. Child suspected to have active TB</td>
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<td>-CXR findings consistent with active or previous untreated, non-healed TB</td>
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<tr>
<td>-Clinical evidence of active TB</td>
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<tr>
<td>3. Child immunosuppressed eg HIV or meds</td>
<td></td>
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<tr>
<td>1. Child at increased risk of disseminated TB</td>
<td>≥10mm</td>
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<tr>
<td>-&lt;4 yrs old, -other medical conditions eg cancer, diabetes, malnutrition</td>
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<tr>
<td>2. Child with increased exposure to active TB</td>
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<tr>
<td>-born in TB-endemic areas</td>
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<tr>
<td>-lives with people born in TB-endemic areas</td>
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<tr>
<td>-Native American children</td>
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<tr>
<td>-frequently exposed to HIV infected adults, homeless, drug users, incarcerated, migrant workers</td>
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<tr>
<td>-travel to TB endemic regions</td>
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<tr>
<td>1. Children ≥4 yrs with no identifiable risk factors</td>
<td>≥15mm</td>
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Preventive treatment:

Prevention of T.B depends on:

1. Preventing contact with patients having active disease.
2. Administration of BCG
   - In Saudi Arabia, administered in the 1st day.
   - In developed countries:
     - Tuberculin-negative children over 5 years should receive BCG vaccination.
3. INH chemoprophylaxis which is indicated in:
   - Tuberculin-negative children less than 5 years (if no more exposure after 3 months PPD-negative = Discontinue.)
# BCG vaccination

**Nature**

BCG is a live attenuated strain of tuberculosis (PPD)

**Efficacy**

Provides 75% protection against tuberculosis for about 15 years

**Indications**

1/ In developed countries (school age children with Mantoux test < 5mm)

2/ In developing countries with a high incidence of tuberculosis (for all neonates)

3/ Individual at risk with Mantoux test < 5mm

**Administration**

Intradermal injection of 0.1 mL in the lateral aspect upper part of left forearm

**Complications**

1/ Local secondary infection

2/ Local lupoid reactions

3/ Abscess / swollen tender draining lymph nodes

4/ Erythema nodosum

5/ Urticaria
Treatment

A. General
Bed rest till the condition improved
Adequate diet

B. Specific: by antituberculosis drugs:
   1. Rifampin (RIF)
   2. Isoniazid (INH)
   3. Pyrazinamide (PZA)
   4. Ethambutol/Ethionamide (ETH)
Treatment

6-months course:

*first 2 months* isoniazid (INH) and rifampicin with pyrazinamide and Ethambutol.

*The Last 4 months* isoniazid and rifampicin.
<table>
<thead>
<tr>
<th>Drugs</th>
<th>Dose</th>
<th>Duration</th>
<th>Mode of action</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptomycin</td>
<td>15 mg/kg</td>
<td>2/12</td>
<td>bactericidal</td>
<td>1/ Hypersensitivity reaction</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>2/ Ototoxic</td>
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<td></td>
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<td></td>
<td>3/ Nephrotoxic</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>15 mg/kg</td>
<td>2/12</td>
<td>Bacteriostatic</td>
<td>Optic Neuritis</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>10 mg/kg</td>
<td>6/12</td>
<td>bactericidal</td>
<td>1/ Hepatotoxic</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>2/ GIT upset</td>
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<td></td>
<td></td>
<td>3/ Flu – like illness</td>
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<td></td>
<td>4/ Brown – red discoloration of all body secretions</td>
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<tr>
<td>Isoniazid (INH)</td>
<td>5 mg/kg</td>
<td>6/12</td>
<td></td>
<td>1/ Hepatotoxic</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2/ Neurotoxic</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>25 mg/kg</td>
<td>2/12</td>
<td></td>
<td>1/ Hepatotoxic</td>
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<td></td>
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<td>2/ Hyperuricemia</td>
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Treatment

- All 4 standard drugs are taken orally
  Dosing for children is weight-based

- INH and RIF are the backbone of treatment

- Hepatitis is biggest concern with TB drugs: adults >> children
  do baseline liver tests for all children on any TB treatment.
Question

- If Mother with Active TB and she wants to breastfed her baby, what is your advice for her?

- A child who had BCG vaccine it might interfere with PPD skin test result, What is last recommendation for PPD with BCG?
Thanks.